Claims

1. Device for treating a crystal with a liquid having a holder for fixing the crystal and at least one micro dosage system, which is arranged in relation to the holder in such a way that it allows applying microdrops of the liquid onto the crystal fixed in the holder.

2. Device according to claim 1, which furthermore comprises a device, by means of which a defined environment can be generated around the crystal during dripping-on of the liquid.

3. Device according to any one of claims 1 or 2, wherein the generation of the defined environment is the generation of a gas stream of defined composition around the crystal.

4. Device according to claims 1 and 3, wherein furthermore the holder is developed in such a way that the gas stream can be led through the holder in such a way that it is directed toward the crystal fixed in the holder.

5. Device according to any one of the preceding claims, wherein the holder consists of a carrier block for a holder capillary having a free support end for the crystal.

6. Device according to claim 5, wherein the holder capillary consists of a micro pipette, wherein a negative pressure can be generated in order to hold the crystal.

7. Device according to any one of claims 5 or 6, wherein the carrier block of the holder contains an integrated gas channel having a mouth end, which is directed toward the support end of the holder capillary.

8. Device according to any one of claims 3 to 7, which furthermore has a gas mixing device, by means of which the composition of the gas stream can be adjusted variably.

9. Device according to claim 8, wherein the gas consists of air having a specific humidity content and the gas mixing device is developed in such a way that by means of it the air humidity can be adjusted.

10. Device according to any one of claims 3 to 9, which furthermore comprises a device for adding a solubilizer, by means of which a solubilizer for a substance to be introduced into the crystal structure of the crystal can be added to the gas stream.

11. Device according to claim 10, which furthermore comprises a device for adjusting the concentration of the solubilizer.

12. Device according to any one of claims 3 to 11, which furthermore comprises a temperature adjusting device, by means of which the temperature of the gas stream can be adjusted variably.

13. Device according to any one of the preceding claims, wherein the micro dosage system is developed in such a way that it can generate microdrops of the liquid to be applied onto the crystal, which have a volume that is smaller than the volume of the crystal.

14. Device according to claim 13, wherein the micro dosage system is developed in such a way that it can generate microdrops having a volume of between 10 and 20 percent of the volume of the crystal and preferably between 5 and 10 percent of the volume of the crystal.

15. Device according to any one of claims 11 or 12, wherein the micro dosage system is developed in such a way that it can generate microdrops having a volume of between 1 nl and 100 pl, preferably between 100 pl and 20 pl, and also preferably between 20 pl and 4 pl.

16. Device according to any one of the preceding claims, wherein the micro dosage system furthermore has a liquid supply system, by means of which different liquids to be dripped onto the crystal can be led to a drop generating part of the micro dosage system in a time-dependently controlled manner.

17. Device according to claim 16, wherein the liquid supply system of the micro dosage system comprises an electrically controllable precision syringe and a duct system, by means of which the precision syringe can be connected with different liquid supply containers and with the drop generating part of the micro dosage system, in order to feed liquid for drop generation to the latter.

18. Device according to any one of the preceding claims, wherein the micro dosage system is developed in such a way that it comprises a piezo pipette forming the drop generation part.

19. Device according to claim 18, wherein the piezo pipette consists of a capillary, which is enclosed by a piezoelectric element.

20. Device according to claim 18 or 19, wherein the micro dosage system furthermore comprises a controlling device electrically connected with the piezo pipette, which is developed in such a way that it allows applying differently shaped voltage pulses, whose shapes regulate the shape and size of the microdrops and whose frequency regulates the frequency of the microdrops, to the piezo pipette.

21. Device according to any one of claims 1 to 17, wherein the micro dosage system comprises a capillary and a micro valve arranged inside the capillary.

22. Device according to claim 21, wherein the micro dosage system furthermore comprises a controlling device for switching the micro valve on and off in order to generate the microdrops.

23. Device according to any one of the preceding claims comprising several micro dosage systems, which are, in relation to the holder, arranged in such a way that they allow applying microdrops of different liquids onto the crystal fixed in the holder.

24. Device according to any one of the preceding claims, wherein the holder is furthermore developed in such a way that it is suitable for fixing a protein crystal.

25. Device according to any one of the preceding claims, wherein the liquid consists of a solution.

26. Device according to claim 21, wherein one or more substance/s to be introduced into the structure of the crystal or to react with the latter is/are solved in the solution.

27. Device according to claim 26, wherein the substance/s consist/s of one or more ligand/s or inhibitor/s.

28. Device according to claim 26, wherein the substance/s contain/s one or more reactant/s, which is/are supposed to react with or in the protein crystal.

29. Device according to claim 25, wherein the solution consists of water, wherein a substance is solved, which is supposed to interact with the protein crystal.

30. Device according to claim 29, wherein the substance consists of an inhibitor or a ligand, which is only hardly soluble in water.

31. Device according to any one of the preceding claims, wherein the liquid contains a cryo buffer.

32. Device according to any one of the preceding claims, wherein the crystal in the holder is not arranged in a liquid, for example the mother solution.

33. Goniometer head having a device according to any one of the preceding claims.

34. X-ray irradiation installation having a device according to any one of the preceding claims.

35. Synchrotron irradiation installation having a device according to any one of claims 1 to 33.

36. Method for treating a crystal with a liquid having the following steps:

- the crystal is fixed, in particular without being surrounded by a liquid environment, and

- microdrops of the liquid are applied onto the crystal.

37. Method according to claim 36, wherein furthermore a defined environment is generated around the crystal during the dripping-on of the microdrops.

38. Method according to claim 37, wherein generating a defined environment comprises generating a gas stream having a defined composition around the crystal.

39. Method according to claim 38, wherein the gas stream consists of an air stream of regulated air humidity.

40. Method according to claim 38, wherein the gas stream is regulated during dripping-on.

41. Method according to any one of claims 39 or 40, wherein the air humidity of the gas stream and the frequency, at which the drops are dripped onto the crystal by means of the micro dosage system, are coordinated during dripping-on in such a way, that the crystal is strained as little as possible, in particular that the volume of the crystal changes by no more than 20%, in particular no more than 10%.

42. Method according to any one of claims 38 to 41, wherein the gas stream comprises a solubilizer of regulated concentration for a substance to be applied onto the crystal.

43. Method according to any one of claims 36 to 42, wherein the volume of the microdrops is smaller than the volume of the crystal.

44. Method according to claim 43, wherein the microdrops of the solution have a volume between 1 nl and 100 pl, preferably between 100 pl and 20 pl, and also preferably between 20 pl and 4 pl.

45. Method according to any one of claims 36 to 44, wherein the crystal is a protein crystal.

46. Method according to any one of claims 36 to 45, wherein the liquid consists of a solution, wherein the solution is optionally heated to a temperature higher than 20°C.

47. Method according to claim 46, wherein the solution contains one or more substance/s containing one or more ligand/s and/or inhibitor/s.

48. Method according to claim 46 or 47, wherein the solution consists of water or an organic solvent or a mixture of organic solvent/s and/or water, in which a substance is contained, which is supposed to interact with the protein crystal.

49. Method according to claim 47 or 48, wherein the substance consists of an inhibitor or ligand, which is only hardly soluble in water.

50. Method according to claim 36, wherein the liquid consists of a cryo buffer.

51. Method according to any one of claims 36 to 50, wherein the gas stream contains one or more substance/s containing one or more ligand/s and/or inhibitor/s.

52. Method according to any one of the preceding claims 36 to 51, wherein the crystal is vapor-plated with solvent, in particular organic solvent, by means of an evaporator.

53. Method for determining a protein crystallographic structure, optionally a complex of a protein and a substance, wherein the method steps according to any one of claims 36 to 52 are conducted and furthermore the crystal is irradiated with X-ray or synchrotron radiation and the diffraction image of the crystal is recorded.

54. Method according to claim 53, wherein the irradiation occurs during the treatment of the crystal with the liquid.

55. Method according to any one of claims 53 or 54, wherein furthermore the intensities of the reflexes of the diffraction image are determined.

56. Method according to any one of claims 53 to 55, wherein furthermore the electron density of the crystal structure is determined by use of the phase information, for example from isomorphic substitution or MAD (multiple anomalous scattering).

57. Method for identifying ligands binding a crystallized protein, wherein (a) a potential ligand is applied onto the crystal by means of a method according to any one of claims 36 to 52, (b) diffraction intensities are measured at intervals of variable length, and (c) said diffraction intensities measured at intervals are compared with respect to their time-dependent sequence.

58. Method for X-ray crystallographic structure determination at high throughput, wherein (a) the crystal/s is/are held ready, preferably in a freely mounted manner, (b) microdrops of a solution containing, for example, at least one ligand are applied onto the preferably freely mounted crystals, (c) the crystals treated according to method step (b) are stored, and (d) the crystals are examined X-ray crystallographically.